The new two-component conformity index formula (TCCI) and dose-volume comparisons of the pituitary gland and tonsil cancer IMRT plans using a linear accelerator and helical Tomotherapy

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ABSTRACT:

BACKGROUND/AIM: To examine the new dose-volume verification tool, called the two-component conformity index formula (TCCI), for tumours of the pituitary gland and tonsil cancer IMRT plans using helical Tomotherapy and a linear accelerator.

MATERIAL AND METHODS: 10 medically inoperable patients – 5 with tumour of the pituitary gland and 5 tonsil cancers – were considered. Tomotherapy and Eclipse plans were compared by DVH analysis and new TCCI analysis including: 1/ the physician's intents for dose distribution in PRVs, 2/ more than one dose-volume constraint for dose distribution in PTV and healthy tissues, and 3/ separation between coverage and excess components.

RESULTS: DVH analysis shows differences for the PTV received doses close to the prescription dose (PD): 1/ in pituitary gland, Eclipse – 61% of PTV volume enclosed by PD and Tomotherapy – 50%, and 2/ in tonsil cancer, Eclipse plans – 44% and Tomotherapy – 55%. These differences were clinically confirmed for tonsil cancer through TCCI analysis. Moreover, TCCI analysis shows better coverage of PTV volume through 90% and 95% isodose levels for Tomotherapy plans. Better high dose region reduction for brain stem and optic chiasm in pituitary gland and middle dose region reduction for parotids and spinal cord in tonsil and dose reduction in healthy tissues reported by TCCI analysis were observed for Tomotherapy plans.

CONCLUSIONS: The usefulness of the information provided means that TCCI could be used as a primary or alternative method of quick dose-volume verification finally supported by advanced DVH analysis.

KEY WORDS: Tomotherapy, IMRT, DVH, Conformity Index

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INTRODUCTION

The main aims of current radiotherapy treatment are to make the high dose volume conform to the planning target volume (PTV) and spare the organs at risk in close proximity [1–3]. The very complex nature of plans derived by current radiotherapy techniques requires a lot of dose-volume-based parameters that have been used to evaluate external beam plans. Apart from the physical dose parameters (e.g. minimum, maximum, median, mean dose and their standard deviation for planning target volume (PTV) and planning risk volumes (PRVs)), equivalent uniform dose is used for evaluation of plans [4–10]. Moreover, several volume-based dosimetric indices called conformity indices (CI) were developed as an additional tool to numerically quantify the dose distributions. CI can be generally defined as

an absolute value resulting from the relationship between PTV and the volume delineated by an isodose. It can also be defined by the ratio of an isodose to another isodose (prescription isodose, reference isodose, minimum isodose, maximum isodose) [11]. The first conformity index was proposed in 1993 by the Radiation Therapy Oncology Group (RTOG) and described in Report 50 of the International Commission on Radiation Units and Measurements (ICRU) [12, 13]. In the last few years, other authors have proposed their formula of the CI with various names [14–19].

However, the multiple indices proposed, as well as the difficulty in interpreting them, raise a number of problems. The use of one numerical value including coverage of PTV and excess volume of the high dose region is not a clear solution. Theoretically the same value of CI can be observed for two different clinical situations. Current ICRU recommendations suggest that four dose-volume constraints can be used for verification of dose distribution in PTV [20]. In this way, only one isodose level according to the CI calculation formula provides an imprecise result of the PTV coverage by the high dose region. Moreover, final values of current CI computations are more dependent on the excess than the coverage component. This dependence provides different results of CI for treatment plans grouped by different volumes or regions of irradiation. The aforementioned shortcomings of the existing CI indices have resulted in its present status, being only an additional tool used for comparison of dose distribution between two plans performed for the same region of irradiation or the same technique. Moreover, existing CI indices are completely insufficient for scoring plans performed for different treatment volumes in the same regions (for example: large and small brain tumours) or techniques (for example: linear accelerator and Tomotherapy IMRT).

In this study a new idea of CI called the two-component conformity index formula (TCCI) is presented. The presented TCCI formula includes: 1/ the physician's intents for dose distribution in PRVs, 2/ more than one dose-volume constraint for dose distribution in PTV and healthy tissues, and 3/ separation between coverage and excess components.

Tomotherapy and linear accelerator IMRT plans of the pituitary gland and tonsil cancers were prepared and evaluated by the TCCI formula. Additionally, functionality of the TCCI computations are discussed in the light of selected CI formulas currently used for plan scoring. Moreover, complementary DVH analysis was performed in which curves and selected parameters of DVH obtained for Tomotherapy and accelerator plans were collected and presented.

MATERIALS AND METHODS

Patients

Ten medically inoperable patients – five with tumour of the pituitary gland and five with oropharyngeal cancer (tonsil, T2N0M0) – previously treated with IMRT at the Greater Poland Cancer Centre between 2005 and 2006 with radical intent were considered for this study. Simulation on the Acuity System (Varian Corp.) and CT scans (Somatom Sensation Open, Siemens Corp.) registered by match point method with MR scans (Sigma Excite 1.5T, GE Corp.) were performed for all patients. The slice thickness was 5 mm in tonsil cancer and 3 mm in pituitary gland tumour. Patients were positioned in a supine position with a thermoplastic mask (Sinmed Corp.) with 5 fixation points for tonsil cancer and 3 fixation points for pituitary gland, respectively. The masks were fixed to the Posifix® IMRT base-plate (Sinmed Corp.)

The dose prescription used for patients with tumour of the pituitary gland was 56 Gy delivered in 28 fractions. In patients with tonsil cancer the following treatment volumes were delineated and dose prescriptions were as follows: 1/ CTV_1 defined as GTV with 5 mm margins received 70 Gy in 35 fractions, 2/ CTV_2 – high-risk lymph node region (ipsilateral II, Ib lymph node regions according to 2003 delineation guidelines consensus [21]) received 60 Gy in 30 fractions, and 3/ CTV_3 defined as ipsilateral (III-V) and contralateral lymph nodes (Ib-V) and retropharyngeal LN received 50 Gy in 25 fractions. Similarly as in pituitary gland cases, to complicate the optimization process different dose prescription was selected in a way that CTV_2 were simulated to receive 70 Gy in 35 fractions.

All contours were delineated on the Soma Vision station (Varian Corp.) by one physician and automatically sent to the Eclipse (Varian Corp) and the HiArt Tomotherapy Planning Station. The PTVs were defined as CTV with 3 mm margins except the first phase of tonsil cancer where a 5 mm margin was added. The brain stem, optic chiasm, optic nerves, eyes and lenses were selected as the planning risk volume (PRV) in pituitary gland cases, and in tonsil cancer cases – the brain stem, parotid glands, spinal cord, oral cavity and larynx. In both cases additional structure surrounding the PTV for dose reduction in healthy tissues was used.

Preparation of treatment plans

6 MV photons were used for the Tomotherapy and the linear accelerator IMRT plan computations. Moreover, the same method of normalization was used in both simulations. In the linear accelerator case the sliding window technique with the 120 millennium MLC was used. Doses and leaf motions were calculated by AAA and Beamlet algorithms respectively [22–25]. The 7-field coplanar (for tonsil) and non-coplanar (for pituitary gland) techniques were used. Orientation of beams was selected individually for every patient by one

physicist. In this way, the tonsil cases included an anterior (gantry rotation set at 0 degrees: GR = 0°), 2 anterior oblique (GR ranges from 30° to 50° and from 310° to 330°), 2 lateral oblique (GR ranges from 90° to 110° and from 250° to 270°), and 2 posterior oblique beams (GR ranges from 140° to 155°

and from 2050 to 2200) and the pituitary gland cases – 2 lateral oblique (GR ranges from 80° to 100° and from 260°0 to 280°), an anterior (GR=0°) and 4 non-coplanar beams in cranial–caudal direction (table rotation was 270° for each beam and GR ranges were: 330° – 350° for first, 20° – 40° for second, 60° – 80° for third, and 110° – 130° for fourth beam). Moreover, the optimal beam orientation from the presented ranges was selected using criteria of the best PTV coverage and PRV sparing.

The same patients (through Dicom transfer) were planned at the Tomotherapy Hi-Art Inc. installation at St-Luc University Hospital in Brussels, Belgium. Beamlet and superposition convolution algorithms were used during Tomotherapy planning. Tomotherapy lasers were moved for each patient to the isocentre positions used in linear accelerator planning (Eclipse). Moreover, 1.0 cm field width was used for dose computations except the PTV_3 of tonsil cancer irradiated to 50 Gy where the width was 2.5 cm. In both situations pitch and modulation factor were set respectively at 0.215 and 2.4.

System constraints, based on the physician's intents, were chosen identically for Tomotherapy and accelerator based IMRT plans. The maximum, minimum and dose for selected percent of volume were used for each PRV and PTV. Weights (Eclipse TPS) or priorities (Tomotherapy TPS) of constraints were changed individually for each patient in order to obtain the best results during optimization of the plans. For example, if for optic chiasm the maximum dose established by the physician was 54 Gy then constraints used in both methods and for all patients were: maximum dose – 50 Gy, and dose absorbed in 10% of the optic chiasm volume – 40 Gy. Table 1 shows the physician's intents and constraints used for pituitary gland and tonsil cancer plans.

DVH analysis

DVH analysis was the first method of dose distribution comparison between Tomotherapy and linear accelerator planning for pituitary gland and tonsil cancer. Mean DVHs with confidence range performed at α=0.05 were computed for each structure and for two planning methods. In computations symmetrical PRVs such as lenses, eyes and optic nerves for pituitary gland cases were included as one structure. Parotids in tonsil cancer cases were grouped as high risk structures (close to PTV2) and low risk (far from PTV2). In Tomotherapy planning the direction blocked method for parotids in tonsil cases and for lenses in pituitary gland cases was used. Moreover, the obtained parameters for the dose distribution corresponding to the physician's intents and to the system constraints were compared.

Two-component conformity index formula (TCCI). General overview

The second method of analysis was the two-component conformity index formula (TCCI). The differences between the dose distribution for two planning methods were evaluated by the TCCI formula dependent on physician's

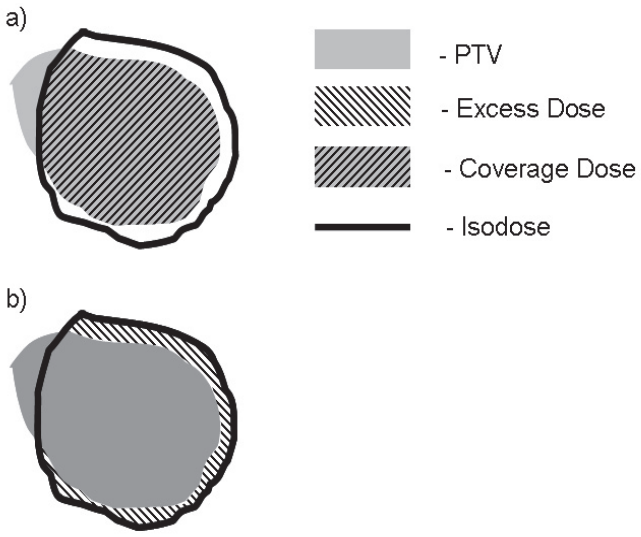

Fig. 1. Schematic view of high dose regions a) covering part of PTV volume and b) received in healthy tissues

intent and described coverage of the PTV and excess dose in healthy tissue components. Moreover, TCCI computations were discussed in the light of current CI formulas. The general formula of the TCCI was expressed as:

$$TCCI(CS;ES) \qquad (1),$$

where CS is the coverage score describing quality of the PTV coverage by more than one isodose and ES is the excess score describing quality of the excess doses in healthy tissues by more than one isodose including PRV influence. The number and value of isodoses included in the TCCI formula are dependent on the physician's specification. Figure 1 shows a schematic view of the CS and ES components included in the TCCI formula.

Coverage Score component of the TCCI

The mathematical formula of the coverage score is dependent on three dose-volume regions of analyzed isodoses specified by a physician. For example, ICRU recommendations suggest four dose-volume dependence regions to verify dose distribution in PTV: 1/ 99% of PTV volume cannot absorb doses lower than 90% of the prescribed dose; 2/ 95% of PTV volume – doses are higher than 95%; 3/ 50% of PTV volume – doses are equal to 100%, and 4/ 1% of PTV volume – doses are lower than 105%.

For the first two regions, described as low doses absorbed in specified high percent volume of PTV, coverage score was described as:

$$CS_i = \frac{V_{PTV,n}}{V_{PTV,tot}} \qquad (2),$$

where $V_{PTV,n}$ is the PTV volume covered by the specified isodose, $V_{PTV,tot}$ is the total volume of the PTV and n is the number of specifications included in the physician's intent – in this example 1 and 2 specifications can be solved by this formula.

For regions including doses close to 100% of the prescription, CS is expressed as follows:

$$CS_i = 1 - \left(\frac{V_{AC,n} - V_{PTV,n}}{V_{PTV,tot}} \right) \qquad (3),$$

where $V_{AC,n}$ is the theoretical volume of the PTV specified by the physician (AC – acceptance criteria) corresponding to the real volume of PTV covered by isodose highlighted in n – specification ($V_{PTV,n}$). In this example n corresponds to 3 specifications.

For regions of high doses absorbed in the specified low percent of PTV volume, the CS formula is:

$$CS_i = 1 - \left(\frac{V_{PTV,n}}{V_{PTV,tot}} \right) \qquad (4),$$

In this example formula 4 could be used in the 4th ICRU specification.

Finally, CS is a product of the CS_n components dependent on the acceptance criteria included in the physician's specification and can be expressed mathematically as:

$$CS = \prod_{i=1}^{n} CS_n \qquad (5),$$

where CS is total coverage score ranging from 0 to 1 (the best value) and n is the number of the acceptance criteria specified by the physician.

Excess Score component of the TCCI

The impact of doses absorbed in healthy tissues and the doses specified by the physician for PRVs was described by a second component of the TCCI formula called Excess Score (ES).

The ES component is dependent on acceptance criteria specified in the physician's intent such as: 1/ the critical doses described as maximum or mean dose or the dose–volume parameter for PRVs (Table 1) and 2/ acceptable excess index (EI) defined as volume of healthy tissues irradiated by specified isodose normalized to the PTV volume. The EI formula was expressed mathematically as follows:

$$EI = \frac{V_{Body,n} - V_{PTV,n}}{V_{PTV,tot}} \qquad (6),$$

where $V_{Body,n}$ and $V_{PTV,n}$ are the volumes of body and PTV covered by n-specified isodose level and $V_{PTV,tot}$ is the total volume of the PTV. In this study five isodose levels (85%, 90%, 95%, 100%, 105%) were used and the acceptable excess (AE) was 1.0, 0.5, 0.3, 0.1, 0.0 respectively for each isodose. For example, if 85% isodose level covered more than two volumes of PTV (EI > 1.0) then the criterion was not realized. In this situation the following formula was used for ES calculation:

$$ES_i = \frac{EI_n - AE_n}{EI_n} \qquad (7),$$

where EI_n is the observed excess index for n-selected isodose level and AE_n is the acceptable value of excess index for n-selected isodose level specified by the physician. In a different situation when $EI_n \leq AE_n$ excess score goes to 0 ($ES_n = 0$).

The second arm of the ES formula was used to verify the agreement between critical doses for PRVs included in intent and corresponding values obtained during plan preparation. Risk index (RI_j) receives 0 and 1 values for each PRV. When $RI_j = 1$ then for PRV_j observed parameters were higher than acceptable. In

Table 1. Physician's intent and system constraints for tumour of the pituitary gland. $D(V_x)$ – dose absorbed in x-percent volume of PRV or PTV. D_{min} – minimum dose, D_{max} – maximum dose, D_{mean} – mean dose

Structure	Physician's Intent[1]	System constraints[2]	
Tumour of the pituitary gland			
PTV	ICRU[3]	D_{min}, D_{max}, $D(V_{50})$: 56 Gy	
Brain stem	$D_{max} < 54$ Gy	D_{max}: 50 Gy; $D(V_{30})$: 20 Gy	
Chiasm	$D_{max} < 54$ Gy	D_{max}: 50 Gy; $D(V_{10})$: 40 Gy	
Optic nerves	$D_{max} < 54$ Gy	D_{max}: 40 Gy; $D(V_{20})$: 20 Gy	
Eyes	$D_{max} < 25$ Gy	D_{max}: 20 Gy; $D(V_5)$: 5 Gy	
Lenses[4]	$D_{max} < 7$ Gy	D_{max}: 4 Gy; $D(V_{50})$: 2 Gy	
Tonsil cancer		**I phase (50 Gy)**	**II phase (20 Gy)**
PTV_1 (to 50 Gy)	ICRU[3]	D_{min}, D_{max}, $D(V_{50})$: 50 Gy	No
PTV_2 (to 20 Gy)	ICRU[3]	No	D_{min}, D_{max}, $D(V_{50})$: 20 Gy
Brain stem	$D_{max} < 54$ Gy	D_{max}: 40 Gy; $D(V_{30})$: 15 Gy	D_{max}: 5 Gy; $D(V_{30})$: 3 Gy
Spinal Cord	$D_{max} < 45$ Gy	D_{max}: 35 Gy; $D(V_{50})$: 25 Gy	D_{max}: 8 Gy; $D(V_{50})$: 6 Gy
Parotids(4)	$D_{mean} < 26$ Gy	D_{max}: 40 Gy; $D(V_{30})$: 15 Gy	D_{max}: 5 Gy; $D(V_{30})$: 2 Gy
Oral cavity	$D_{mean} < 35$ Gy	D_{max}: 45 Gy; $D(V_{30})$: 30 Gy	D_{max}: 10 Gy; $D(V_{30})$: 5 Gy
Larynx	$D_{mean} < 35$ Gy	D_{max}: 45 Gy; $D(V_{50})$: 20 Gy	No

[1] Intents depended on the total prescribed dose: 56 Gy in pituitary gland and 70 Gy in tonsil cancer
[2] Only weights or priority constraints were changed
[3] ICRU recommendations: $D(V_{99}) \geq 90$ %, $D(V_{95}) \geq 95$ %, $D(V_{50}) \geq 100$ %, $D(V_1) \leq 105$ %
[4] Direction blocked method used in Tomotherapy planning

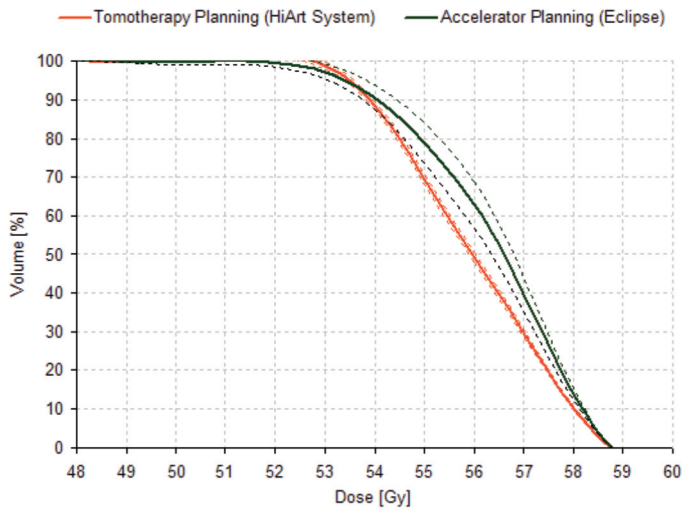

Fig. 2. Mean dose-volume histograms of the planning target volumes received for five patients with tumour of the pituitary gland. Red line presents DVH received for Tomotherapy and black presents Eclipse planning. Solid lines present mean DVHs and dashed present ranges of confidence performed at α =0.05

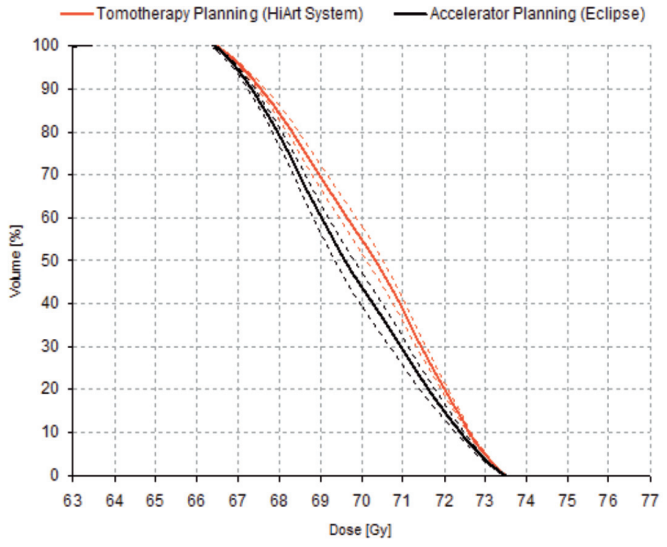

Fig. 3. Mean dose-volume histograms of the planning target volumes received for five tonsil cancer patients. Red line presents DVH received for Tomotherapy and black presents Eclipse planning. Solid lines present mean DVHs and dashed present ranges of confidence performed at α=0.05

another way, when observed parameters were lower than acceptable, then risk index goes to 0. For example, if acceptable mean dose for parotids specified by the physician was D_{mean} ≤26 Gy and observed mean dose was lower than acceptable, then risk index goes to 0.

Finally, excess score was expressed mathematically as follows:

$$ES = \frac{1}{n}\sum_{i=1}^{n} ES_i + \sum_{j=1}^{k} RI_j \qquad (8),$$

where n = number of isodose levels, ES_i = excess score calculated for i-level of isodose, and RIj = risk index calculated for PRV_j.

Excess score receives values from 0 (the best value) to

$$k + \frac{1}{n}\sum_{i=1}^{n} ES_i$$

where k is the number of PRVs included in calculations.

RESULTS

Figures 2 and 3 show the differences between doses in PTV delivered by Tomotherapy and linear accelerator (Eclipse) methods for tumour of the pituitary gland and tonsil cancer. The red line presents DVH received for Tomotherapy and black presents Eclipse planning. Solid

lines present mean DVHs and dashed present ranges of confidence level performed at α=0.05.

The selected PRVs dose comparisons for Tomotherapy and Eclipse plans in pituitary gland and tonsil groups are shown in Figures 4 and 5. Figure 4 shows brain stem, optic chiasm optic nerves and eyes dose-volume histograms for Tomotherapy and Eclipse planning in tumour of the pituitary gland, and Figure 5 shows spinal cord and high and low risk parotids in tonsil cancer. Similarly as in Figures 2 and 3, the same methods of visualization (colours and lines) were used.

Table 2 shows results of the coverage score computations for PTVs of pituitary gland tumour and CTV_2 irradiated to 70 Gy of tonsil cancer cases. Highlighted rows (black colour) split the table into two groups. The first column includes number (n) of criterion level included in CS_i computations (formulas 2, 3, 4) presented in corresponding rows. Criterion levels were defined as: 1/ for n=1 99% of PTV volume cannot absorb doses lower than 90% of prescribed dose (PD); 2/ for n=2 95% of PTV

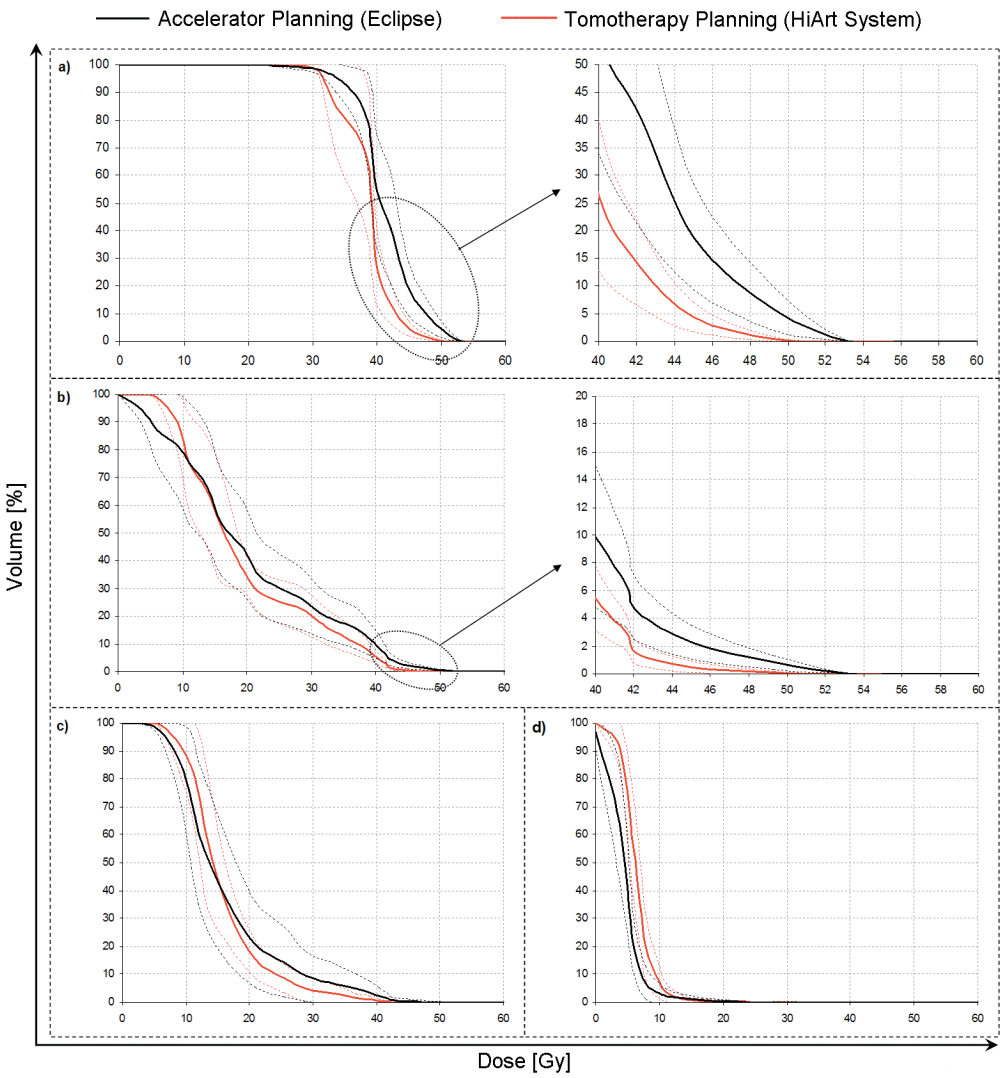

Fig. 4. Selected planning risk volumes dose comparison for a) optic chiasm, b) brain stem, c) optic nerves and d) eyes. Each plot contains mean DVHs (solid lines) with corresponding confidence range (dashed lines) for 5 pituitary gland cases. For a) and b) structures significant dose difference regions were marked and enlarged. Red lines present histograms for Tomotherapy and black, Eclipse. α=0.05

absorbed doses not lower than 95% of PD; 3/ for n=3 50% of PTV absorbed doses equal to or higher than PD (100%) and 4/ for n=4 1% of PTV absorbed doses lower than 105% of PD. Bolded rows show CS result (product of received CS_i, formula 5) for each patient and groups of delivery method, respectively.

Table 3 shows results of excess score (ES) computations for PTVs delineated for tumour of the pituitary gland and CTV2 of tonsil cancer. Table 3 like Table 2 was split into two groups. The first column includes isodose level (D [%]) used for excess index (EI) computations (formula 6) and number (n) of criterion level included during ESi computations (formula 7). EI and ESi are presented, corresponding to D[%] and n rows. Criterion levels were defined as: 1/ for n=1, EI is lower than 1 for volume enclosed by 85% isodose; 2/ for n=2, EI≤0.5 for 90% isodose; 3/ for n=3, EI≤0.3 for 95% isodose; 4/ for n=4, EI≤0.1 for 100% isodose and 5/ for n=5, EI=0 for 105%

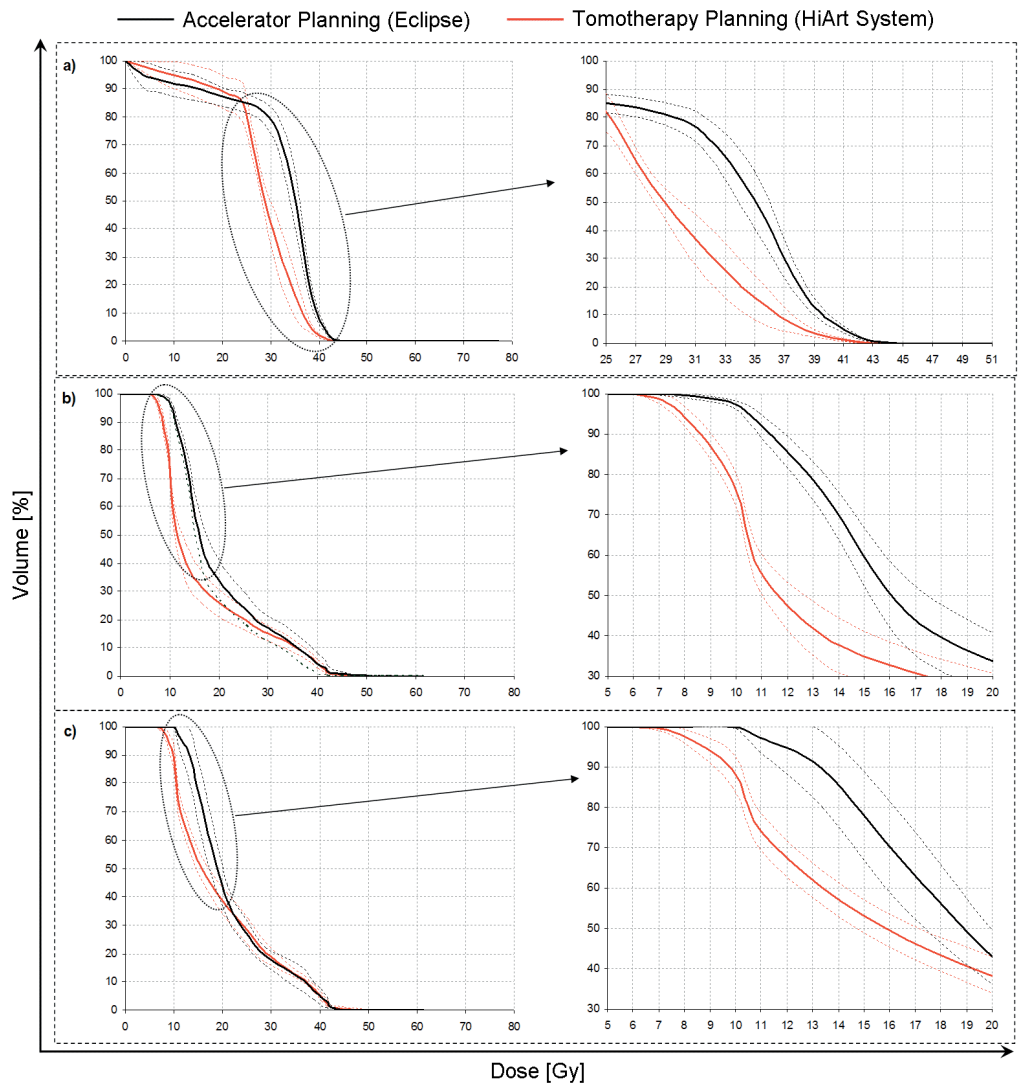

Fig. 5. Selected planning risk volumes dose comparison for a) spinal cord, b) parotids low risk and c) parotids high risk. Each plot contains mean DVHs (solid lines) with corresponding confidence range (dashed lines) for 5 tonsil cancer patients. For each presented structure significant dose difference regions were marked and enlarged. Red lines present histograms for Tomotherapy and black, Eclipse. $\alpha = 0.05$

isodose. Bolded rows show ES result (formula 8) for each patient and delivery method groups, respectively. Figures 6 and 7 show dependence between absorbed doses and excess index (Table 3) obtained for Tomotherapy and Eclipse plans in pituitary gland and tonsil cancer respectively.

DISCUSSION

DVH analysis for PTVs and PRVs

General DVH analysis shows good coverage of PTVs for both Tomotherapy and Eclipse plans. However, statistically significant differences between the two delivery modalities were observed for PTV volumes enclosed with dose range from 98% to 102%. For pituitary gland cases, larger volume of PTV absorbed this range of doses as a result of Eclipse planning ($p=0.01$). The reverse situation was observed in tonsil cancer cases – doses close to the prescribed dose were absorbed in a larger volume of PTV as a result of Tomotherapy

planning (p=0.015). For example: 1/ in the pituitary gland group, Eclipse plans provide 61% of PTV volume enclosed by the prescribed dose, and Tomotherapy plans – 50% (Figure 2); 2/ in the tonsil group, Eclipse plans – 44%, and Tomotherapy – 55% (Figure 3). Moreover, lower standard deviation for Tomotherapy than for Eclipse (0.7 Gy versus 1.1 Gy in tumour of pituitary gland and 0.8 Gy versus 1.2 Gy in tonsil cancer) suggest better dose homogeneity for the first method. Similar results were observed in other studies of Tomotherapy and linear accelerator plan comparisons [26, 27].

All plans successfully realized the intents specified by the physician, related to accepted doses in PRVs. Although satisfactory dose sparing in PRVs is realized by two compared modalities, for structures located close to the PTVs such as the optic chiasm or brain stem in pituitary gland cases with partially overlapping PTVs, and parotids in tonsil cases, better dose distributions for Tomotherapy plans were observed. For example, in pituitary gland cases, the high dose region was significantly better reduced through Tomotherapy plans in brain stem (p=0.02) and optic chiasm (p=0.013). High dose region for PRVs was defined as the range from D_{max} – 75% of D_{max} to D_{max}. The maximum dose (D_{max}) specified by the physician was 54 Gy for both structures. As a result the high dose region included part of PRV volumes enclosed by doses from 40.5 Gy to 54 Gy (see Figures 4a – optic chasm, 4b – brain stem and enlarged regions). In tonsil cases, the middle dose region (near to the median dose) for parotids and spinal cord was better reduced through Tomotherapy than Eclipse plans. The p-values were 0.031 for low risk and 0.04 for high risk parotids, and 0.023 for spinal cord. Middle dose regions were established from 5 Gy to 20 Gy for parotids and from 25 Gy to 43 Gy for spinal cord (see Figures 5a – spinal cord, 5b – low risk parotids and 5c – high risk parotids with enlarged regions). No significant differences for other PRVs such as optic nerves, eyes and lenses for pituitary gland and oral cavity and larynx for tonsil cancer were observed. Figures 4c and 4d show example DVHs for optic nerves and eyes in the pituitary gland group. Our results correspond to other works where dose reduction in PRVs was evaluated [28–30].

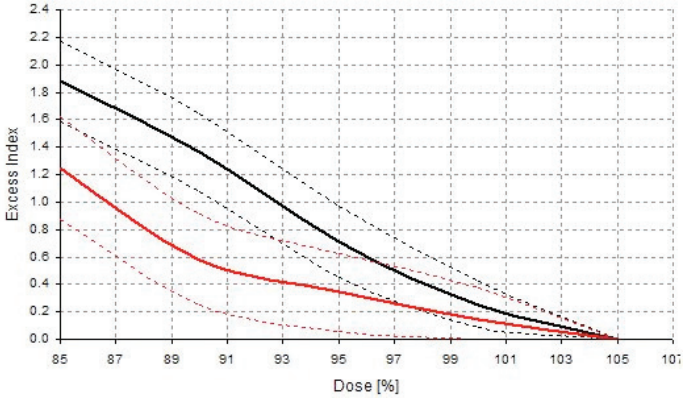

Fig. 6. Dependence between excess index and absorbed doses [%] for Tomotherapy (red colour) and Eclipse (black colour) in pituitary gland group. Solid lines present means and dashed confidence range performed at $\alpha = 0.05$

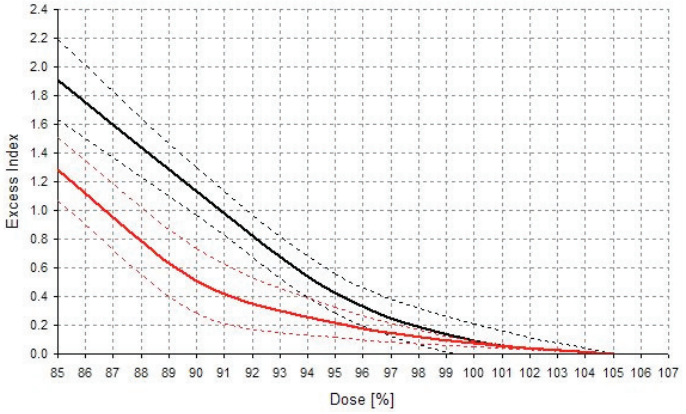

Fig. 7. Dependence between excess index and absorbed doses [%] for Tomotherapy (red colour) and Eclipse (black colour) in tonsil cancer group. Solid lines present means and dashed confidence range performed at $\alpha = 0.05$

TCCI analysis

Observed results of coverage score (Table 2) confirmed good coverage of PTVs for both Tomotherapy and Eclipse plans (mean CS range from 0.936 to 1). However, some discrete differences, not detected during DVH analysis, were observed. In pituitary gland cases the worst results for criteria 1 and 2 (see Table 2 description), described as low dose distribution in PTV for Eclipse plans, were obtained. For example, for criterion 2 (95% of PTV cannot absorb doses lower than 95% of the prescribed dose) in pituitary gland cases all patients received an ideal CS_i value equal to 1 for Tomotherapy, and

Table 2. Coverage Score (CS) computations for PTVs delineated for tumour of the pituitary gland and CTV_2 of tonsil cancer. Highlighted rows (black colour) split table into two respective groups. The first column includes number (n) of criterion level included in CS_i computations (formulas 2, 3, 4) presented in corresponding rows. Criterion levels were defined as: 1/ for n=1 99% of PTV volume cannot absorb doses lower than 90% of prescribed dose (PD); 2/ for n=2 95% of PTV absorbed doses not lower than 95% of PD; 3/ for n=3 50% of PTV absorbed doses equal to or higher than PD (100%) and 4/ for n=4 1% of PTV absorbed doses lower than 105% of PD. Bolded rows show CS result (product of received CSi, formula 5) for each patient and groups of delivery method, respectively

Patient:	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
n	**Tomotherapy planning (HiArt System)**					**Linear accelerator planning (Eclipse)**				
	tumor of the pituitary gland									
1	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
2	1.000	1.000	1.000	1.000	1.000	1.000	0.948	0.943	0.947	1.000
3	0.992	1.000	0.997	0.999	1.000	1.000	1.000	1.000	1.000	1.000
4	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
CS:	0.992	1.000	0.997	0.999	1.000	1.000	0.948	0.943	0.947	1.000
Mean CS: 0.968			0.998					0.968		
	tonsil cancer PTV_2 (to 70Gy)									
1	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
2	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
3	1.000	1.000	1.000	1.000	1.000	0.939	0.916	0.932	0.941	0.952
4	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
CS:	1.000	1.000	1.000	1.000	1.000	0.939	0.916	0.932	0.941	0.952
Mean CS:			1.000					0.936		

for Eclipse, second, third and fourth patients received lower values of CS_i – 0.948 , 0.943, 0.947, respectively (Table 2).

Differences in PTV volumes enclosed with dose range from 98% to 102% observed during DVH analysis were plain described by TCCI analysis. Only a few statistically significant differences were also clinically significant because some of the observed differences during DVH analysis were above clinical specification. For example, in the pituitary gland group lower mean volume of PTV received prescribed doses for Tomotherapy (50%) than for Eclipse plans (61%). This was not clinically significant because 50% of PTV absorbing the prescribed dose was an acceptable value specified by the physician. In analysis for individual patients, CS_i values received for this criterion were close to 1 in Tomotherapy – 0.992, 1.000, 0.997, 0.999, 1.000 for first to fifth patient respectively (Table 2). These results suggest that doses received by 50% of volume were near to the prescribed dose.

In tonsil cancer the opposite situation was observed. 55% of mean PTV volume absorbed the prescribed dose for Tomotherapy and 44% for Eclipse plans. In this situation statistically significant differences were confirmed clinically. Doses absorbed by 50% of the PTV for Eclipse plans were significantly lower than the prescribed dose. As a result each patient received a relatively small CS_i value – 0.939, 0.916, 0.932, 0.941, 0.952 respectively for the first to fifth patient (Table 2).

For each patient and both delivery methods, doses absorbed in PRVs were lower than doses specified as acceptable criteria. In this situation the risk index component (RIj) included in excess score computations (formula 8) goes to 0. Only high doses received in healthy tissues not specified as PRVs affected final ES values.

The region of normal tissues, enclosed by high doses, was defined using five isodose levels: 85%, 90%, 95%, 100%, 105%. Acceptable excess indices defined by the physician

Table 3. Excess score (ES) computations for PTVs delineated for tumour of the pituitary gland and CTV2 of tonsil cancer. Highlighted rows (black colour) split table into two respective groups. First column includes isodose level (D [%]) used for excess index (EI) computations (formula 6) and number (n) of criterion level included during ES_i computations (formulas 7). EI and ES_i are presented, corresponding to D[%] and n rows respectively. Criterion levels were defined as: 1/ for n=1, EI is lower than 1 for volume enclosed by 85% isodose; 2/ for n=2, EI≤0.5 for 90% isodose; 3/ for n=3, EI≤0.3 for 95% isodose; 4/ for n=4, EI≤0.1 for 100% isodose and 5/ for n=5, EI=0 for 105% isodose. Bolded rows show ES result (formula 8) for each patient and delivery method groups

Patient:	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
	Tomotherapy planning (HiArt System)					**Linear accelerator planning (Eclipse)**				
	tumor of the pituitary gland									
D [%]	**Excess Index for Tomotherapy**					**Excess Index for Eclipse**				
85	1.1	1.6	0.8	1.8	0.9	2.2	2.1	1.3	2.0	1.8
90	0.3	1.2	0.6	0.4	0.4	1.6	1.6	0.8	1.5	1.2
95	0.1	0.9	0.3	0.2	0.2	0.5	1.1	0.4	0.9	0.6
100	0.0	0.5	0.0	0.1	0.0	0.2	0.5	0.2	0.3	0.0
105	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
n	**Excess Scores Component for Tomotherapy**					**Excess Scores Component for Eclipse**				
1	0.13	0.37	0.00	0.44	0.00	0.54	0.51	0.25	0.50	0.45
2	0.00	0.59	0.15	0.00	0.00	0.69	0.69	0.41	0.66	0.60
3	0.00	0.66	0.13	0.00	0.00	0.40	0.73	0.23	0.67	0.53
4	0.00	0.80	0.00	0.00	0.00	0.42	0.82	0.43	0.69	0.00
5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
ES:	0.03	0.61	0.07	0.11	0.00	0.51	0.69	0.33	0.63	0.39
Mean ES:	0.16					0.51				
	tonsil cancer PTV_2 (to 70Gy)									
D [%]	**Excess Index for Tomotherapy**					**Excess Index for Eclipse**				
85	1.2	1.2	1.2	1.7	1.0	1.8	1.5	2.0	2.4	2.0
90	0.6	0.7	0.6	0.1	0.6	1.1	0.9	1.2	1.4	1.2
95	0.0	0.2	0.2	0.3	0.3	0.5	0.2	0.5	0.6	0.4
100	0.0	0.1	0.1	0.1	0.1	0.0	0.0	0.3	0.0	0.1
105	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
n	**Excess Scores Component for Tomotherapy**					**Excess Scores Component for Eclipse**				
1	0.18	0.18	0.19	0.42	0.00	0.43	0.33	0.50	0.58	0.49
2	0.15	0.30	0.17	0.00	0.12	0.53	0.41	0.58	0.64	0.57
3	0.00	0.00	0.00	0.00	0.11	0.39	0.00	0.36	0.47	0.33
4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.68	0.00	0.00
5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
ES:	0.08	0.12	0.09	0.10	0.07	0.34	0.19	0.53	0.42	0.35
Mean ES:	0.09					0.36				

for specified isodoses were: 1/ 85% isodose could cover the volume of normal tissues corresponding to PTV volume (EI≤1); 2/ 90% isodose (EI≤0.5); 3/ 95% isodose (EI≤0.3); 4/ 100% isodose (EI≤0.1) and 5/ doses higher than 105% could not cover normal tissues and can be absorbed only in PTV volume (EI=0). Lower excess scores for Tomotherapy plans

were observed for each comparison. The dependence between absorbed doses and excess index obtained for Tomotherapy and Eclipse plans is graphically illustrated in Figures 6 and 7. Moreover, decreasing dependence between excess score and volume of PTV was observed. For example, mean ES values were: 0.16 for Tomotherapy and 0.51 for Eclipse plans in the pituitary gland group (mean PTV volume was 19.8 cm^3) and 0.09 for Tomotherapy and 0.36 for Eclipse plans in the tonsil cancer group (mean PTV volume was 107.1 cm^3).

Detailed results obtained during the TCCI analysis were not possible in current CI formulas where only one isodose level was used without dose in PRV evaluation. Including more than one isodose level for dose evaluation in PTV and healthy tissues not specified as PRVs and including impact of the dose absorbed in PRVs provides more precise conclusions during evaluation or comparison of plans. Moreover, splitting coverage and excess components allows clearer presentation of the results than in current CI formulas where one value describes two effects. Finally, the dependence of the physician's intents makes the TCCI formula a more elastic tool applied to clinical routine. The TCCI formula is experimentally used as a second tool for verification of plans prepared for patients routinely treated in the Greater Poland Cancer Centre. A special computer program based on mathematical expression included in the TCCI formula was created. This program compiled TCCI results for all DVH data previously exported as ASCII files from the Eclipse Planning Station. However, the usefulness of delivered information means that the TCCI could be used as a primary or alternative method of quick dose-volume verification finally supported by advanced DVH analysis.

CONCLUSIONS

General DVH analysis shows similar coverage of PTV volume for Tomotherapy and Eclipse plans except for some statistically significant differences for PTV volumes receiving doses close to the prescription dose (in the pituitary gland, Eclipse plans provide 61% of PTV volume enclosed by the prescribed dose, and Tomotherapy plans 50%; and in tonsil cancer, Eclipse plans – 44%, Tomotherapy – 55%). These differences were clinically confirmed for tonsil cancer through TCCI analysis. Moreover, TCCI analysis shows better coverage of PTV volume through 90% and 95% isodose levels for Tomotherapy plans.

Clinically accepted dose sparing in PRVs for both plan preparation methods was produced. For Tomotherapy plans, better high dose region reduction for brain stem ($p=0.02$) and optic chiasm ($p=0.013$) in the pituitary gland and middle dose region reduction for parotids (high risk $p=0.04$, low risk $p=0.031$) and spinal cord ($p=0.023$) in tonsil cases was observed. Moreover, TCCI analysis shows better dose reduction in healthy tissues not specified as PRVs. In the pituitary gland excess score was 0.16 for Tomotherapy and 0.51 for Eclipse plans. In tonsil cancer – 0.09 and 0.36 for Tomotherapy and Eclipse IMRT plans respectively.

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